Obesity and Insulin Resistance from Impaired Maternal Glucose Metabolism

Impaired **maternal glucose metabolism** during pregnancy is directly related to risk of **obesity** and **insulin resistance** in offspring.

General Information	
Broad Focus Area	Obesity and altered physical development
Background and Justification	Determining the strength of the association between impaired maternal glucose metabolism during pregnancy and overweight in children is a timely issue because the prevalence of overweight among women of childbearing age has increased,[1] which is a risk factor for impaired maternal glucose metabolism.[2] The offspring of mothers who have type 1 diabetes are at increased risk of overweight, and this effect is often evident as early as 4 years of age.[3] Other studies, where mothers with gestational diabetes were grouped together with type 1 and type 2 diabetics, have also shown increased risk of overweight in offspring.[3] On the basis of these observations, offspring of mothers with gestational diabetes, or lesser degrees of impaired glucose metabolism, are suspected of being at increased risk of obesity, but there is little data available to address the issue, and those data that are available have extremely limited statistical power.[3,4]
Prevalence/ Incidence	The prevalence of overweight among children is greater than 16% among children aged 6 years or more, and this prevalence has increased over the past 40 years.[5,6] Overweight children are at increased risk for being overweight in adulthood,[7] and are associated with increased risk of type 2 diabetes, hypertension, and coronary artery disease.[8] Furthermore, being overweight as a child increases the risk of developing type 2 diabetes before the age of 21 years.[9] The total prevalence of diabetes in women aged 20-39 years is 1.7% and 6% among those aged 40-49 years.[10] Among reproductive-aged women with diabetes, about one-third (35.4%) of women younger than 40 years and about one-quarter (26.7%) of those aged 40 years or older did not know that they had the disease.[10] About 4-7% of pregnancies are complicated by gestational diabetes.[2] Assuming Impaired Glucose Tolerance is of two types 1) "impaired fasting glucose (IFG)" or 2) "impaired glucose tolerance (IGT)," depending on the test used to diagnose it: - In a cross-section of U.S. adults aged 40 to 74 years tested from 1988 to 1994, 33.8 percent had IFG, 15.4 percent had IGT, and 40.1 percent had pre-diabetes (IGT or IFG or both). Applying these percentages to the 2000 U.S. population, about 35 million adults aged 40 to 74 would have IFG, 16 million would have IGT, and 41 million would have pre-diabetes.[11] - Based on data from the 1999-2000 National Health and Nutrition Examination Survey, approximately 2% of U.S. adults between 20 and 39 years of age are affected by impaired fasting glucose, a type of impaired glucose metabolism.[12]
Economic Impact	Because child obesity is a risk factor for adult obesity, child obesity contributes to the more than $40 billion annual cost of obesity in the United States.[13]

Exposure Measures			Outcome Measures	
Primary/	- Physician or self report of pre-		***Primary/***	

Maternal	existing or gestational diabetes - Blood glucose and HgbA1C - Oral glucose tolerance test (potential study procedure) - Serum lipid profile - Serum insulin or related sample (e.g., C-peptide) - Genetic sample (for exploration of potentially relevant genes such as VNTR insulin, glucokinase)		***Maternal***	
Methods	Blood sample - medical records review - interview - physical exam - anthropometry		Methods	
Life Stage	Prenatal & birth		Life Stage	
Secondary/ Maternal			***Primary/Child***	<u>Insulin resistance</u>: - Serum insulin levels, Glucose levels, HgbA1C <u>Obesity</u>: - IGF - Body size and habitus - Body composition
Methods			Methods	Blood sample, Physical exam anthropometry, body composition
Life Stage			Life Stage	Birth & periodic

Important Confounders/Covariates	
Lipid profile	Increased lipid levels are associated with an increased risk of insulin resistance[14]
Glucokinase mutation	Glucokinase mutation is associated with increased risk of maturity onset diabetes of the young (MODY) [15]
Hormone levels such as cortisol, growth hormone, insulin-like growth factors	Elevated levels of these and other hormones are associated with obesity and insulin resistance in children [16]
Genetic markers for obesity	Certain genetic markers increase risk of obesity
Parents' body mass indices	BMI and obesity are associated with certain genetic markers.[17]
Family history of diabetes and obesity	A family history of diabetes and obesity increases child's risk.[18, 17]
Lifestyle factors	Less active lifestyles would increase risk of obesity and insulin resistance.[9]
Nutrition	Poor nutritional and high caloric diet would increase risk of obesity and insulin resistance [19]
Socio-economic status and demographics	Children of lower economic status, ethnic and racial groups (particularly Native Americans, Hispanics, African Americans, and Asians) are at higher risk of obesity and insulin resistance.[18]

Population of Interest		Estimated Effect that is Detectable
All pregnant women and their offspring.		About 4-7% of pregnancies are complicated by gestational diabetes.[2] Assuming 100,000 children, and an exposure prevalence of 5%: Smallest detectable relative risk for obesity (prevalence 10%, using 30 kg/m2 definition) ~ 1.2 Smallest detectable relative risk for metabolic syndrome (assumed prevalence 0.4%) ~ 1.7

Other Design Issues	
Cost/Complexity of Data Collection	Addressing this hypothesis based on obesity and insulin resistance measures at later life-stages may be adversely impacted by attrition of study subjects.

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